Correspondence

Lung angiotensin converting enzyme activity in monocrotaline pulmonary hypertension

SIR,—We have shown that lung tissue angiotensin converting enzyme (ACE) activity was reduced in rats with pulmonary hypertension induced by a single injection of monocrotaline (*Thorax* March 1982, p 198). Lafranconi and Huxtable, however (April 1983, p 307), have suggested that this decrease in specific activity of ACE was due to an increase in total lung protein and not to an actual reduction in the total ACE activity in the lung. We have therefore recalculated our data in terms of total ACE activity per lung (nmol/min/lung). The mean (SD) value for the control group (n = 10) was 1379·9 (492·9), and for the group treated with monocrotaline (n = 7) 657·4 (225·2). Thus there was a significant decrease in total lung ACE activity in the rats treated with monocrotaline (t = 3·597, $p < 0·005$). In a recent experiment[1] we measured angiotensin II immunoreactive material in right ventricular and aortic blood derived from control rats (n = 7) and rats given a single injection of monocrotaline (n = 5). In the control rats the mean (SD) angiotensin II levels (pg/ml) in the right ventricle and aorta were 435 (115) and 738 (164) respectively. These values were significantly reduced to 72 (36) and 153 (83) respectively in rats treated with monocrotaline. Plasma renin activity was higher in the monocrotaline treated rats than controls and could be not implicated in the decreased angiotensin II levels. Lung ACE levels were significantly decreased in the monocrotaline treated rats and we suggest that this was responsible for the reduced angiotensin II values. It is important to realise that whereas we gave our rats a single injection of monocrotaline (60 mg/kg body weight) Lafranconi and Huxtable administered monocrotaline in the drinking water (20 mg/l) for up to three weeks. Accordingly, it is not clear what dose was received by individual rats, and there must have been considerable variation between their animals. This difference in experimental design may account for our differing results.

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[1] Keane PM, Kay JM. Diminished plasma angiotensin II response to hemorrhagic stress in rats with pulmonary hypertension. *Clin Invest Med* (in press).

**This letter was sent to the authors, who reply below.

SIR,—From the angiotensin converting enzyme (ACE) activities reported per mg lung protein by Dr JM Kay and others (February 1982, p 88), and per lung by Keane and Kay above, it can be calculated that their monocrotaline treated lungs have undergone a mild 15% increase in protein mass. Why do our reports differ in the degree of pulmonary hyperplasia, and the level of ACE activity in the lung? This could be due to differences in procedure. Kay and his coworkers gave a single injection of monocrotaline, 60 mg/kg subcutaneously, to rats averaging 113 g in weight. We exposed 50 g rats to drinking water containing 20 mg/l of monocrotaline. The difference in the weight of the animals used may be more important than the route of administration. We know that as rats get older they become less susceptible to pyrrolizidine poisoning. Unlike Dr Kay and his colleagues, we have never seen right ventricular hypertrophy in the absence of lung hyperplasia following injections of monocrotaline (intraperitoneal or subcutaneous) as shown by the table:

Monocrotaline (given by a single injection) in relation to size of lung and right ventricle in rats (means (SD) of the results for at least five animals)

Monocrotaline dose (mg/kg)		*Organ: body weight ratio (% control)*	
		Lung	*Right ventricle and septum*
Intraperitoneal	25	100 (20)	70 (14)
	50	150 (20)	164 (28)
	100	160 (20)	186 (36)
Subcutaneous	25	100 (10)	80 (7)
	50	110 (20)	107 (20)
	100	160 (30)	200 (33)

Drs Keane and Kay comment on our subacute route of administration. The advantages of this method are: it is milder in that as little as five days of the protocol will produce the same degree of pulmonary hyperplasia 21 days later as will a single injection of 60 mg/kg of monocrotaline; there is no overt liver toxicity; and the protocol avoids pulmonary oedema and inflammatory changes in the heart and lungs which are unrelated to the degree of right ventricular damage. A disadvantage of the method is that there is some variability in the dose of monocrotaline received by individual rats. However, our technique produces consistent right ventricular hypertrophy, and we use this hypertrophy as the reference point for determining the degree of damage. The consistency of the technique is shown by the fact that the ratio of right ventricular weight to that of the left ventricle plus septum is 0·561 (0·144) (mean (SD) for 36 animals).[1] This is identical to the value reported by Kay *et al* of 0·558 (0·113). As has been elegantly demonstrated by Kay and Heath,[2] there is a constant relationship between the increase in right ventricular weight, pulmonary arterial systolic blood pressure, and arterial medial thickness after exposure to pyrrolizidine. We have taken, as these authors have proposed, right ventricular weight as an index of the progression of hypertensive disease.

We would conclude the following: (i) The difference in

observations between ourselves and Dr Kay and his colleagues may be explicable by differences in the route of administration of monocrotaline and the size of the animals used. (ii) We find lung hyperplasia, right ventricular hypertrophy, and reductions in serotonin transport in the absence of changes in lung total ACE. (iii) If hyperplasia of an organ occurs, the expression of enzyme activities on a total organ basis is appropriate. (iv) We have observed right ventricular hypertrophy only after the development of lung hyperplasia. It is implied by Drs Keane and Kay that right ventricular hypertrophy may be obtained after monocrotaline administration in the absence of lung hyperplasia. This is an important statement, and should be appropriately documented (no data on organ weights are presented in their report), as it has a bearing on hypotheses concerning the inducement of hypertrophy.

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[1] Huxtable R, Ciaramitaro D, Eisenstein D. The effect of a pyrrolizidine alkaloid, monocrotaline, and a pyrrole, dehydroretronecine, on the biochemical functions of the pulmonary endothelium. *Mol Pharmacol* 1978;**14**:1189–203.
[2] Kay JM, Heath D. *Crotalaria spectabilis:* the pulmonary hypertension plant. Springfield: Charles C Thomas, 1969.

Purulent pericarditis with tamponade: a rare complication of pectus repair

SIR,—Since the introduction of antibiotics purulent pericarditis has become uncommon and most cases occur after cardiac surgery. However, we have recently encountered such a case following surgery for pectus excavatum.

A 22 year old woman developed bilateral pleural effusions one month after classical repair of severe asymmetrical pectus excavatum. She also presented with clinical features of a right calf vein thrombosis. She was anticoagulated with heparin, but sustained a cardiorespiratory arrest 45 days after operation and was thought to have sustained a massive pulmonary embolism. When the chest was opened, however, the pericardium was found to contain a tense collection of pus. This was drained, with immediate improvement in the circulation. Her subsequent postoperative course was uneventful.

Occasional reports of purulent pericarditis following oesophageal perforation have appeared[1] and on one occasion this presented as pericardial tamponade.[2] Purulent pericarditis rarely occurs after surgery when the pericardium is not opened[3] and to our knowledge this is the first report of pyogenic tamponade complicating repair of pectus excavatum.

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[1] Bozer AY, Saylam A, Ersoy U. Purulent pericarditis due to perforation of oesophagus with foreign body. *J Thorac Cardiovasc Surg* 1974;**67**:590–2.
[2] Welch TG, White TR, Lewis RP, Altieri PI, Vasko JS, Kilman JW. Oesophagopericardial fistula presenting as cardiac tamponade. *Chest* 1972;**62**:728–31.
[3] Bulkley BN, Klacsmann PG, Hutchins GM. A clinicopathological study of post-thoracotomy purulent pericarditis. A continuing problem of diagnosis and therapy. *J Thorax Cardiovasc Surg* 1977;**73**:408–12.

Notices

British Thoracic Society

7–9 May 1984
Joint Meeting with Australian Thoracic Society in Adelaide (meeting with chest physicians in Sydney 4 or 5 May)
4–6 July 1984
Brighton: Metropole Hotel (NB abstracts required by *19 April*)
6–7 December 1984
London: Kensington Town Hall
3–5 July 1985
York University

Correction

Effect of naloxone on circadian rhythm in lung function

We regret that in the paper by Dr S Al-Damluji and others (December 1983, pp914–8) there is an error in the caption to table 2: "in five patients" should be "in six patients."